

EPILEPTIC SEIZURES AND EEG FEATURES IN JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS

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Abstract – Introduction: Juvenile systemic lupus erythematosus is more incident in female affecting different systems including the central nervous system. The aim of this study was to check the incidence of seizures and electroencephalographic features in these patients. **Method:** It was analyzed all patients with juvenile systemic lupus erythematosus referred to the Pequeno Príncipe Hospital in Curitiba, PR, Brazil, in the year of 2007. The patients were submitted to EEG and subdivided into two groups according to the presence or absence of epileptic seizures. Mann-Whitney statistical test was used. **Results:** Forty-nine cases were included, there were 73.45% female, with an age between 3 and 28 years ($\mu=17.00$ years; $s=5.01$ years). Seizures (13/26.50%) were the most frequent manifestation followed by headache (13/26.50%) and ischemic stroke (6/12.25%). Cerebral vasculites were the most frequent alteration in neuroimage. The abnormalities of EEG were characterized by asymmetry of the electric cerebral activity, diffuse disorganized background activity, focal epileptiform discharges in the right central-temporal region, generalized paroxysmal of 3 Hz spike-waves, and bursts of theta-delta slowness activity in the right parietal-occipital region. The statistic analysis showed no significantly difference between age of onset of symptoms and the risk of seizures ($p 0.675$) as well as between time of the disease and the risk of seizures ($p 0.436$). **Conclusion:** Neurologic manifestations, in special epileptic seizures, are frequent in systemic lupus erythematosus. Age of onset of symptoms and the time of disease did not increase the risk of epileptic seizures in this disease.

KEY WORDS: juvenile systemic lupus erythematosus, epileptic seizures, neurologic manifestation.

Crises epilépticas e características do EEG em pacientes com lúpus eritematoso sistêmico juvenil

Resumo – Introdução: Lupus eritematoso sistêmico juvenil é doença mais freqüente no sexo feminino afetando múltiplos sistemas, incluindo o sistema nervoso central. O objetivo deste estudo foi avaliar a incidência de crises epilépticas e de alterações eletrencefalográficas nestes pacientes. **Método:** Foram avaliados todos os pacientes com lupus eritematoso sistêmico juvenil encaminhados para o Hospital Pequeno Príncipe em Curitiba, PR, Brasil, no ano de 2007. Os pacientes foram submetidos a EEG e subdivididos em 2 grupos conforme a presença ou não de crises epilépticas. A análise foi realizada através do teste estatístico de Mann-Whitney. **Resultados:** 49 casos foram incluídos, sendo 73,45% do sexo feminino, com idade variando entre 3 e 28 anos ($\mu=17,00$ anos; $s=5,01$ anos). Crises epilépticas (13/26,50%) foram a manifestação neurológica mais freqüente, seguidas de cefaléia (13/26,50%) e acidente vascular cerebral isquêmico (6/12,25%). Vasculite cerebral foi a alteração de imagem mais freqüente. As alterações no EEG foram caracterizadas por assimetria da atividade elétrica cerebral, desorganização difusa da atividade de base, descargas epileptiformes na região centro-temporal direita, paroxismos generalizados de espícula-onda à 3 Hz e surtos de onda lenta na faixa delta-teta na região parieto-occipital direita. A análise estatística não demonstrou diferença significativa entre a idade de início dos sintomas e risco de crise epiléptica ($p 0,675$) e nem entre tempo de evolução da doença e risco de crise epiléptica ($p 0,436$). **Conclusão:** Manifestações neurológicas, particularmente crises epilépticas, são freqüentes no lupus eritematoso sistêmico juvenil. A idade de início dos sintomas e o tempo de duração da doença não aumentam o risco de crises epilépticas nesta doença.

PALAVRAS-CHAVE: lúpus eritematoso sistêmico juvenil, crises epilépticas, manifestações neurológicas.

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Juvenile systemic lupus erythematosus (JSLE) is a multisystem disorder characterized by serum antibodies against a wide variety of nuclear, cytoplasm and serum protein antigens¹. There is a female preponderance of 8:1 which is thought to be due to a synergistic effect of female hormones¹. The JSLE symptoms begin in childhood in 20% of the patients and usually occurs in children with more than 8 years². In addition there are racial differences in the incidences of JSLE ranging from 31/100000 among oriental females to 4.4/100000 in white females, with black females falling in between at 19.8/100000³. In 1982, the American College of Rheumatology has listed 11 diagnostic criteria and patients that fulfilled four of these are considered to have JSLE⁴.

JSLE affects different systems and organs including the central nervous system and its clinical variability turns it into a more complex disease. The commonest neurological manifestations are seizures and psychosis followed by focal disorders such as hemiplegia, paraplegia, chorea, intention tremor, cranial nerves deficits, internuclear ophthalmoplegia, sensory losses, transverse myelitis and polyneuritis⁵. In spite of the fact that 10 to 75% of adult patients with JSLE had experienced neurological complications with or without behavioral, cognitive and psychiatric disturbances, there's few data about these manifestations in children⁶. The main problem with the diagnosis of neuropsychiatric JSLE is the lack of a gold standard in laboratory examinations to corroborate the clinical judgement⁷.

The aim of this study was to check the incidence of seizures, neurologic manifestations and electroencephalographic (EEG) abnormalities in patients with the diagnosis of JSLE. This paper was approved by the ethics committee of Pequeno Principe Hospital and parental written informed consent was obtained for publication.

METHOD

The study was based on the analysis of 49 patients referred to the Pediatric Rheumatology Department of Pequeno Principe Hospital in Curitiba, PR, Brazil, in the year of 2007 with the diagnosis of SLE. All patients fulfilled the diagnostic criteria of American Academy of Rheumatology (AAR). Medical records from all patients provided the following data: age, sex, disease duration, neurological manifestations, image exams and electroencephalographic register.

They were subdivided into two groups according to the presence or absence of epileptic seizures. Twenty-nine patients were submitted to EEG with minimal duration of 40 minutes. Electrodes were positioned according to the International 10-20 System. Whenever necessary sleep was induced by chloral hydrate 8% administered orally. All EEG tracings were obtained in 21 channel digital equipment and photic stimulation was used with all patients. The exam was analyzed by two neurophysiologists.

Mann-Whitney statistical test was used for independents data to study the relationship between age of onset of symptoms and the risk of seizures and the relationship between time of disease and the risk of seizures.

RESULTS

Out of the 49 cases studied, there were 36 (73.45%) females with a varying age between 3 and 28 years ($\mu=17.00$ years; $s=5.01$ years). The mean time of the disease duration at recruitment were 5.15 years, with a range of 6 months to 15 years ($s=3.95$ years). Analyzing the neurological manifestations, 41 (83.60%) patients had at least one clinical sign of central nervous system disease. Seizures (13/26.50%) were the most frequent manifestation followed by headache, ischemic stroke, tremor, psychosis, VI nerve palsy, dysarthria, chorea and anorexia (Table).

Neuroimaging exams were performed in 71.40% of the cases. Thirteen patients had a CT, eighteen a MRI and four had both exams. Cerebral vasculitis were observed in 10 cases (20.40%), cerebral atrophy in 4 (8.15%) and ischemic stroke in 6 (12.25%). EEG was performed in 29 patients (59.20%) and was considered normal in 82.75% of the cases. The abnormalities of EEG were characterized by asymmetry of the electric cerebral activity with left frontal-central slowness (1/3.44%), diffuse disorganized background activity (1/3.44%), focal epileptiform discharges with sharp waves in the right central-temporal region (1/3.44%), generalized paroxysmal of 3Hz spike-waves (1/3.44%) and bursts of theta-delta slowness activity in the right parietal-occipital region (1/3.44%).

The patients were divided into two groups considering the presence or absence of seizures. The group without seizures had 36 (73.45%) patients, 28 (77.75%) of whom were female. The mean age of JSLE first symptom was 11.90 years ($s=3.30$ years) and the mean time of disease evolu-

Table. Neurological manifestations in juvenile systemic lupus erythematosus.

Manifestation	n	%
Seizures	13	26.50
Headache	13	26.50
Ischemic stroke	6	12.25
Tremor	3	6.10
Psychosis	2	4.10
VI nerve palsy	1	2.05
Dysarthria	1	2.05
Chorea	1	2.05
Anorexia	1	2.05
Total	41	83.60

Note: 41 (83.60%) patients had at least one clinical sign of central nervous system disease.

tion was 4.85 years ($s=3.75\%$). The group with seizures had 13 patients (26.55%), 8 (61.55%) of whom were female. The mean age of JSLE first symptom was 11.85 years ($s=2.05$ years) and the mean time of disease evolution was 6.00 years ($s=4.50$ years).

The analysis with Mann-Whitney statistical test showed no significant difference between age of onset of symptoms and the risk of seizures ($p 0.675$) as well as between time of the disease and the risk of seizures ($p 0.436$).

DISCUSSION

The word lupus means "wolf" in latin and was used since 1.230 d.C. as a medical term to describe dermatological findings that resembled a malar erythema in the wolf. The first clear description of lupus erythematosus was by Biett and was reported by his student Cazenave under the term erythema centrifugum in 1833⁸. In 1872 Kaposi subdivided for the first time lupus into the discoid and systemic forms and introduced the concept of systemic disease with a potentially fatal outcome⁹. Neuropsychiatry symptoms in SLE were already recognized in the pioneering descriptions of Kaposi and Osler, but were considered rare. They are now recognized to occur up to 75% of patients and are a leading cause of morbidity and mortality⁷.

The variability of neurological manifestations in JSLE patients is huge. In the majority of pediatric series reviews, seizures appear to be the most prominent central nervous system (CNS) manifestation¹. According to Hussain et al.¹, in his study of 24 patients with JSLE, seizures were the most frequent neurologic manifestation, followed by encephalopathy, psychosis and headache. This data corroborate with our findings except from the high frequency of ischemic stroke reported in our study.

The evaluation of CNS involves a variety of laboratory and neurodiagnostic methods, such as EEG, computed tomography, magnetic resonance imaging, single photon emission computed tomography (SPECT), positron emission tomography (PET) and blood and spinal fluid analysis. None of these are diagnostic of or specific for JSLE. In this disease both cerebral CT and MRI are frequently normal⁶⁻⁸. However, Waterloo et al.¹⁰ reported cortical and subcortical CT lesions in almost 50% of his patients and cerebral infarctions in 12% of his SLE cases. Hussain et al.¹ described cerebral atrophy alone, atrophy with infarcts, multiple infarcts, basal ganglia calcifications as the most common CT lesions. In 1999, Schibata et al.¹¹ described an 11-year-old girl with CNS lupus with diffuse lesions including on the cerebral white matter, bilateral basal ganglia, thalami and brainstem. Cerebral vasculitis was the most common CNS lesion observed in our series. The neurologic manifesta-

tions in CNS vasculitis are multiples and have relationship with topography lesion.

EEG changes are known to take place in 50% of patients with connective tissue disorders, especially with JSLE^{12,13}. Some workers have used quantitative EEG to diagnose cerebral lupus and found it to be more sensitive than MRI and CT scanning¹.

Colamussi et al.¹⁴ detected EEG abnormalities in 60% of JSLE patients with CNS manifestations. Lampropoulos et al.¹² revealed an increased prevalence of temporal slow activity in JSLE patients. Khedr et al.¹⁵ demonstrated focal EEG abnormalities in his study, involving rather slowing (13.0%) than sharp spikes (6.6%). He also showed more EEG abnormalities in patients with overt neurological manifestations than in group without.

In the comparative study of our sample there was no significant difference between age of onset of symptoms and the risk of seizures ($p 0.675$) as well as between time of the disease and the risk of seizures ($p 0.436$). It is necessary to improve this sample in order to evaluate the veracity of this tendency.

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